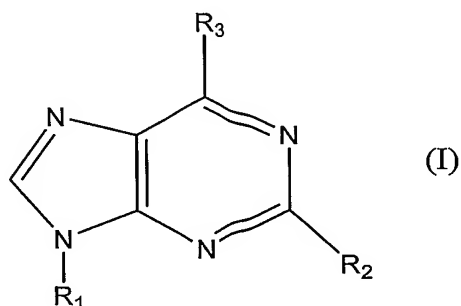


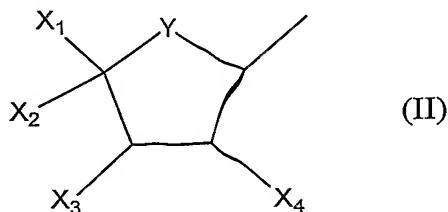
**CLAIMS:**

1. A method for the treatment of accelerated bone resorption in a mammal subject, the method comprises administering to said subject in need of said treatment an amount of an A<sub>3</sub> adenosine receptor agonist (A<sub>3</sub>AR agonist), the amount being effective to inhibit bone resorption.
2. The method of Claim 1, wherein said mammal is a human subject.
3. The method of Claim 1, for the treatment of inflammation induced bone resorption.
4. The method of Claim 3, for the treatment of bone resorption induced by inflammatory arthritis.
5. The method of Claim 1, wherein said treatment comprises oral administration of A<sub>3</sub>AR agonist to said subject in need.
6. The method of Claim 5, wherein said treatment comprises administration of A<sub>3</sub>RA agonist to said subject once or twice daily.
7. The method of Claim 1, wherein said A<sub>3</sub>AR agonist is a compound within the scope of the general formula (I):



wherein,

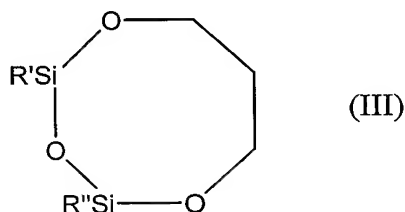
- R<sub>1</sub> represents an alkyl, hydroxyalkyl, carboxyalkyl or cyanoalkyl or a group of the following general formula (II):



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in which:

- Y represents an oxygen, sulfur or CH<sub>2</sub>;
- X<sub>1</sub> represents H, alkyl, R<sup>a</sup>R<sup>b</sup>NC(=O)- or HOR<sup>c</sup>-, wherein
  - R<sup>a</sup> and R<sup>b</sup> may be the same or different and are selected from the group consisting of hydrogen, alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl or are joined together to form a heterocyclic ring containing two to five carbon atoms; and
  - R<sup>c</sup> is selected from the group consisting of alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl;
- X<sub>2</sub> is H, hydroxyl, alkylamino, alkylamido or hydroxyalkyl;
- X<sub>3</sub> and X<sub>4</sub> represent independently hydrogen, hydroxyl, amino, amido, azido, halo, alkyl, alkoxy, carboxy, nitrilo, nitro, trifluoro, aryl, alkaryl, thio, thioester, thioether, -OCOPh, -OC(=S)OPh or both X<sub>3</sub> and X<sub>4</sub> are oxygens connected to >C=S to form a 5-membered ring, or X<sub>2</sub> and X<sub>3</sub> form the ring of formula (III):

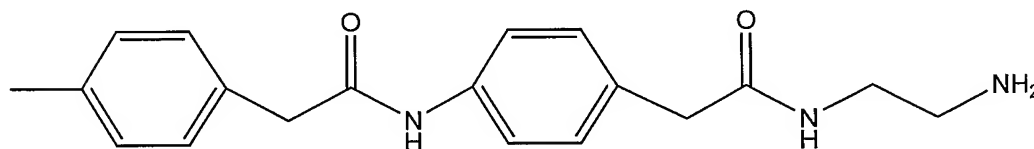


where R' and R'' represent independently an alkyl group;

- R<sub>2</sub> is selected from the group consisting of hydrogen, halo, alkylether, amino, hydrazido, alkylamino, alkoxy, thioalkoxy, pyridylthio, alkenyl, alkynyl, thio, and alkylthio; and
- R<sub>3</sub> is a group of the formula -NR<sub>4</sub>R<sub>5</sub> wherein
  - R<sub>4</sub> is a hydrogen atom or a group selected from alkyl, substituted alkyl or aryl-NH-C(Z)-, with Z being O, S, or NR<sup>a</sup> with R<sup>a</sup> having the above meanings; wherein when R<sub>4</sub> is hydrogen then
  - R<sub>5</sub> is selected from the group consisting of R- and S-1-phenylethyl, benzyl, phenylethyl or anilide groups unsubstituted or substituted in one or more positions with a substituent selected from the group consisting of alkyl, amino, halo,

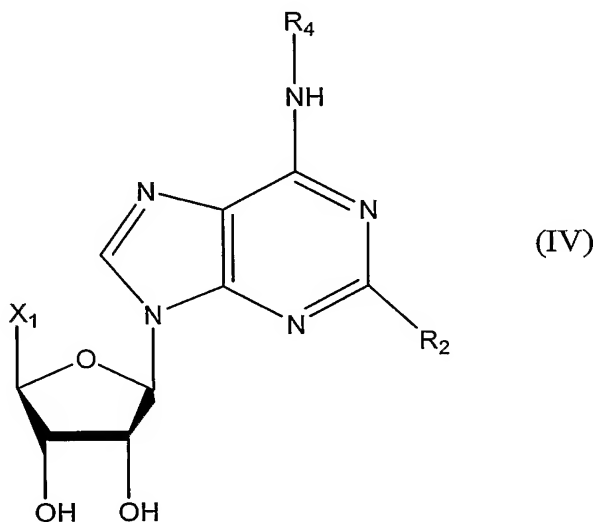
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haloalkyl, nitro, hydroxyl, acetoamido, alkoxy, and sulfonic acid or a salt thereof; benzodioxanemethyl, fururyl, L-propylalanyl- aminobenzyl,  $\beta$ -alanylaminobenzyl, T-BOC- $\beta$ -alanylaminobenzyl, phenylamino, carbamoyl, phenoxy or cycloalkyl; or  $R_5$  is a group of the following formula:



or when  $R_4$  is an alkyl or aryl-NH-C(Z)-, then,  $R_5$  is selected from the group consisting of heteroaryl-NR<sup>a</sup>-C(Z)-, heteroaryl-C(Z)-, alkaryl-NR<sup>a</sup>-C(Z)-, alkaryl-C(Z)-, aryl-NR-C(Z)- and aryl-C(Z)-; Z representing an oxygen, sulfur or amine; or a physiologically acceptable salt of the above compound.

8. The method of claim 1, wherein said A<sub>3</sub>AR agonist is a nucleoside derivative of the general formula (IV):



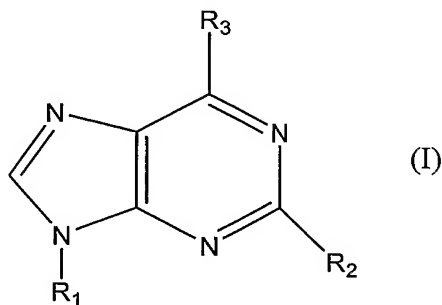
wherein  $X_1$ ,  $R_2$  and  $R_4$  are as defined in claim 3, and physiologically acceptable salts of said compound.

9. The method of Claim 1 wherein said A<sub>3</sub>AR agonist is selected from N<sup>6</sup>-2-(4-aminophenyl)ethyladenosine (APNEA), N<sup>6</sup>-(4-amino-3-iodobenzyl) adenosine- 5'-(N-methyluronamide) (AB-MECA), N<sup>6</sup>-(3-iodobenzyl)-adenosine- 5'-N- methyluronamide (IB-MECA) and 2-chloro-N<sup>6</sup>-(3-iodobenzyl)- adenosine- 5'-N-methyluronamide (Cl-IB-MECA).

10. The method of claim 9, wherein said A<sub>3</sub>AR agonist is IB-MECA.

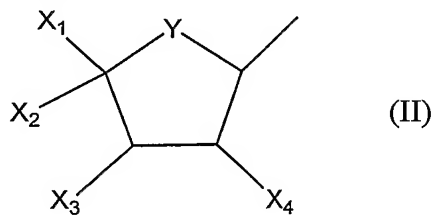
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11. A pharmaceutical composition for the treatment of accelerated bone resorption, the composition comprising an amount of an  $A_3AR$  agonist, the amount being effective to inhibit bone resorption in a mammal subject.
12. The pharmaceutical composition of Claim 11, in a dosage form suitable for oral administration.
13. The pharmaceutical composition of Claim 11, for the treatment of inflammation induced bone resorption.
14. The pharmaceutical composition of Claim 13, for the treatment of bone resorption induced by inflammatory arthritis.
15. The pharmaceutical composition of Claim 11, wherein said  $A_3AR$  agonist is a compound within the scope of the general formula (I):



wherein,

- $R_1$  represents an alkyl, hydroxyalkyl, carboxyalkyl or cyanoalkyl or a group of the following general formula (II):



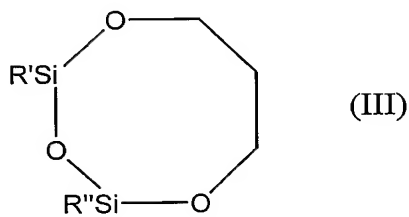
in which:

- $Y$  represents an oxygen, sulfur or  $CH_2$ ;
- $X_1$  represents H, alkyl,  $R^a R^b NC(=O)-$  or  $HOR^c-$ , wherein
  - $R^a$  and  $R^b$  may be the same or different and are selected from the group consisting of hydrogen, alkyl, amino, haloalkyl, aminoalkyl,

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BOC-aminoalkyl, and cycloalkyl or are joined together to form a heterocyclic ring containing two to five carbon atoms; and

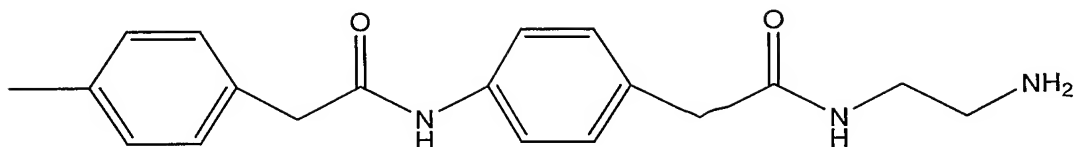
- $R^c$  is selected from the group consisting of alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl;
- $X_2$  is H, hydroxyl, alkylamino, alkylamido or hydroxyalkyl;
- $X_3$  and  $X_4$  represent independently hydrogen, hydroxyl, amino, amido, azido, halo, alkyl, alkoxy, carboxy, nitrilo, nitro, trifluoro, aryl, alkaryl, thio, thioester, thioether, -OCOPh, -OC(=S)OPh or both  $X_3$  and  $X_4$  are oxygens connected to  $>C=S$  to form a 5-membered ring, or  $X_2$  and  $X_3$  form the ring of formula (III):



where  $R'$  and  $R''$  represent independently an alkyl group;

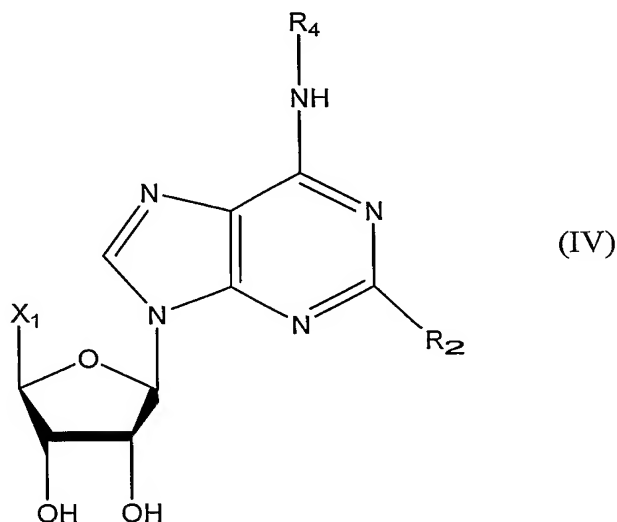
- $R_2$  is selected from the group consisting of hydrogen, halo, alkylether, amino, hydrazido, alkylamino, alkoxy, thioalkoxy, pyridylthio, alkenyl, alkynyl, thio, and alkylthio; and
- $R_3$  is a group of the formula  $-NR_4R_5$  wherein
  - $R_4$  is a hydrogen atom or a group selected from alkyl, substituted alkyl or aryl-NH-C(Z)-, with Z being O, S, or  $NR^a$  with  $R^a$  having the above meanings; wherein when  $R_4$  is hydrogen than
  - $R_5$  is selected from the group consisting of R- and S-1-phenylethyl, benzyl, phenylethyl or anilide groups unsubstituted or substituted in one or more positions with a substituent selected from the group consisting of alkyl, amino, halo, haloalkyl, nitro, hydroxyl, acetoamido, alkoxy, and sulfonic acid or a salt thereof; benzodioxanemethyl, fururyl, L-propylalanyl- aminobenzyl,  $\beta$ -alanylaminobenzyl, T-BOC- $\beta$ -alanylaminobenzyl, phenylamino, carbamoyl, phenoxy or cycloalkyl; or  $R_5$  is a group of the following formula:

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or when  $R_4$  is an alkyl or aryl-NH-C(Z)-, then,  $R_5$  is selected from the group consisting of heteroaryl-NR<sup>a</sup>-C(Z)-, heteroaryl-C(Z)-, alkaryl-NR<sup>a</sup>-C(Z)-, alkaryl-C(Z)-, aryl-NR-C(Z)- and aryl-C(Z)-; Z representing an oxygen, sulfur or amine; or a physiologically acceptable salt of the above compound.

16. The pharmaceutical composition of Claim 11, wherein said A<sub>3</sub>AR agonist is a nucleoside derivative of the general formula (IV):



wherein  $X_1$ ,  $R_2$  and  $R_4$  are as defined in claim 3, and physiologically acceptable salts of said compound.

17. The pharmaceutical composition of Claim 11, wherein said A<sub>3</sub>AR agonist is selected from N<sup>6</sup>-2- (4-aminophenyl)ethyladenosine (APNEA), N<sup>6</sup>-(4-aminophenyl-3-iodobenzyl) adenosine- 5'-(N-methyluronamide) (AB-MECA), N<sup>6</sup>-(3-iodobenzyl)-adenosine-5'-N- methyluronamide (IB-MECA) and 2-chloro-N<sup>6</sup>-(3-iodobenzyl)- adenosine-5'-N-methyluronamide (Cl-IB-MECA).

18. The pharmaceutical composition of Claim 11, wherein said A<sub>3</sub>AR agonist is IB-MECA.

19. Use of an A<sub>3</sub>AR agonist for the preparation of a pharmaceutical composition for the treatment of accelerated bone resorption.

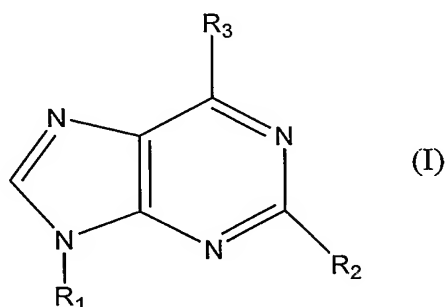
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20. The use of Claim 19, for the preparation of a composition suitable for oral administration.

21. The use of Claim 20, for the preparation of a composition the treatment of inflammation induced bone resorption.

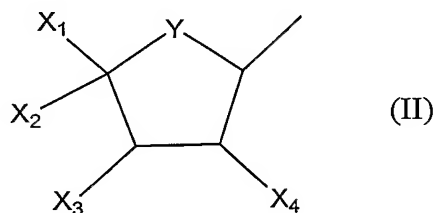
22. The use of Claim 21, wherein said composition is for the treatment of bone resorption induced by inflammatory arthritis.

23. The use of Claim 19, wherein said  $A_3AR$  agonist is a compound within the scope of the general formula (I):



wherein,

-  $R_1$  represents an alkyl, hydroxyalkyl, carboxyalkyl or cyanoalkyl or a group of the following general formula (II):

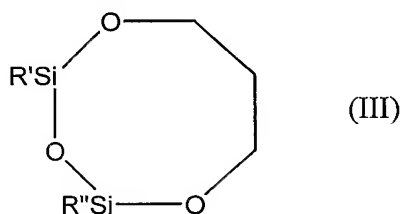


in which:

- Y represents an oxygen, sulfur or  $CH_2$ ;
- $X_1$  represents H, alkyl,  $R^a R^b NC(=O)-$  or  $HOR^c-$ , wherein
  - $R^a$  and  $R^b$  may be the same or different and are selected from the group consisting of hydrogen, alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl or are joined together to form a heterocyclic ring containing two to five carbon atoms; and
  - $R^c$  is selected from the group consisting of alkyl, amino, haloalkyl, aminoalkyl, BOC-aminoalkyl, and cycloalkyl;

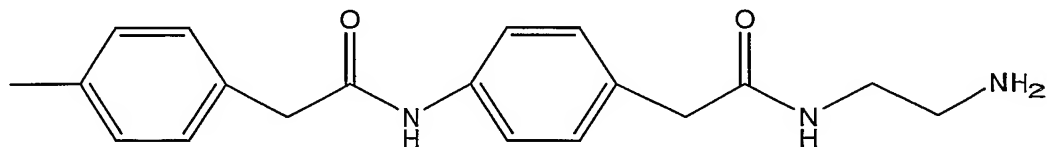
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- $X_2$  is H, hydroxyl, alkylamino, alkylamido or hydroxyalkyl;
- $X_3$  and  $X_4$  represent independently hydrogen, hydroxyl, amino, amido, azido, halo, alkyl, alkoxy, carboxy, nitrilo, nitro, trifluoro, aryl, alkaryl, thio, thioester, thioether, -OCOPh, -OC(=S)OPh or both  $X_3$  and  $X_4$  are oxygens connected to  $>C=S$  to form a 5-membered ring, or  $X_2$  and  $X_3$  form the ring of formula (III):



where  $R'$  and  $R''$  represent independently an alkyl group;

- $R_2$  is selected from the group consisting of hydrogen, halo, alkylether, amino, hydrazido, alkylamino, alkoxy, thioalkoxy, pyridylthio, alkenyl; alkynyl, thio, and alkylthio; and
- $R_3$  is a group of the formula  $-NR_4R_5$  wherein
- $R_4$  is a hydrogen atom or a group selected from alkyl, substituted alkyl or aryl-NH-C(Z)-, with  $Z$  being O, S, or  $NR^a$  with  $R^a$  having the above meanings; wherein when  $R_4$  is hydrogen than
- $R_5$  is selected from the group consisting of R- and S-1-phenylethyl, benzyl, phenylethyl or anilide groups unsubstituted or substituted in one or more positions with a substituent selected from the group consisting of alkyl, amino, halo, haloalkyl, nitro, hydroxyl, acetoamido, alkoxy, and sulfonic acid or a salt thereof; benzodioxanemethyl, fururyl, L-propylalanyl- aminobenzyl,  $\beta$ -alanylaminobenzyl, T-BOC- $\beta$ -alanylaminobenzyl, phenylamino, carbamoyl, phenoxy or cycloalkyl; or  $R_5$  is a group of the following formula:

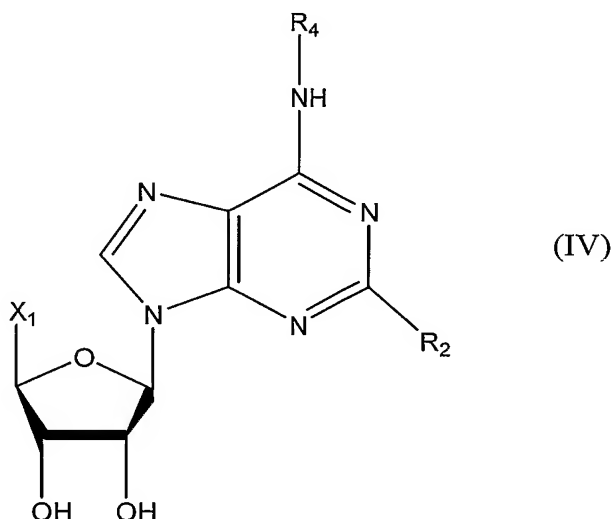




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or when  $R_4$  is an alkyl or aryl-NH-C(Z)-, then,  $R_5$  is selected from the group consisting of heteroaryl-NR<sup>a</sup>-C(Z)-, heteroaryl-C(Z)-, alkaryl-NR<sup>a</sup>-C(Z)-, alkaryl-C(Z)-, aryl-NR-C(Z)- and aryl-C(Z)-; Z representing an oxygen, sulfur or amine; or a physiologically acceptable salt of the above compound.

24. The use of Claim 19, wherein said A<sub>3</sub>AR agonist is a nucleoside derivative of the general formula (IV):



wherein  $X_1$ ,  $R_2$  and  $R_4$  are as defined in claim 3, and physiologically acceptable salts of said compound.

25. The use of Claim 19, wherein said A<sub>3</sub>AR agonist is selected from N<sup>6</sup>-2-(4-aminophenyl)ethyladenosine (APNEA), N<sup>6</sup>-(4-amino-3-iodobenzyl) adenosine- 5'-(N-methyluronamide) (AB-MECA), N<sup>6</sup>-(3-iodobenzyl)-adenosine- 5'-N- methyluronamide (IB-MECA) and 2-chloro-N<sup>6</sup>-(3-iodobenzyl)- adenosine- 5'-N-methyluronamide (Cl-IB-MECA).

26. The use of Claim 19, wherein said A<sub>3</sub>AR agonist is IB-MECA.